

### **REMARKS**

Claims 1 and 8-9 have been amended. Support for the amendments can be found throughout the specification (e.g., pages 78-80) and original claims (e.g., claims 8-9 and 11). No new matter has been introduced. Applicants submit that the amendments are made merely to expedite allowance of claims directed to most commercially relevant embodiments of the present invention. Applicants reserve the right to pursue claims of similar or differing scope in the future.

Applicants respectfully request reconsideration in view of the following remarks. Issues raised by the Examiner will be addressed below in the order they appear in the prior Office Action.

#### **Election/Restriction**

The Office Action has acknowledged Applicants' election, with traverse, of Group I (claims 1-11) and the species election of mRNA in the Response filed on October 2, 2006.

#### **Priority**

The Office Action states that "the priority date for some limitations (i.e. tooth decay, pyorrhea, and periodontitis) of claim 11 is the present application filing date of November 18, 2003 and the priority date for some limitations of claim 11 (i.e. HIV and gingivitis) is November 18, 2002. All other claims presently have a priority date of January 29, 2002." Office Action, page 4, lines 15-18. Applicants reserve the right to traverse the Examiner's assertion until allowable subject matter is found; at which point, Applicants will provide supportive priority documents if deemed necessary.

#### **Information Disclosure Statement (IDS)**

The Examiner has considered and initialed the Information Disclosure Statement submitted on April 15, 2005.

#### **Objection to the Specification**

First, the Examiner asserts that reference numbers 20 and 22 for Figure 22 are not described. In response, Applicants have amended the specification (e.g., the paragraph bridging pages 65 and 66) to correct this deficiency.

Second, the Examiner asserts that the trademark GenChip® should be capitalized wherever it appears and be accompanied by the generic terminology. In response, Applicants have amended the specification to obviate this objection.

Claim Rejections under 35 U.S.C. § 112, First Paragraph

Claims 1, 5-6, and 8-11 are rejected under 35 U.S.C. § 112, first paragraph, as allegedly failing to comply with the written description requirement. Applicants respectfully traverse this rejection to the extent it is maintained over the claims as amended.

The Office Action asserts that "[t]he invention as claimed encompasses all known genes associated with all oral diseases, all genes which may potentially be associated with all oral diseases in the future, and any yet to be discovered oral diseases. The claimed invention does not include any structural information regarding the genes." Office Action, page 6, last paragraph.

Applicants respectfully disagree and submit that the specification amply teaches the claimed invention. Nevertheless, solely to expedite prosecution of the application, Applicants have amended claim 1 to more particularly point out the claimed method. Claim 1 as amended recites a method for diagnosing an oral cancer in a patient, comprising: a) obtaining a biological sample from a patient; b) determining the expression level of a plurality of genes associated with an oral cancer in the biological sample, thereby producing a test expression profile; and c) comparing the test expression profile with at least one signature expression profile of the plurality of genes selected from Table 1 indicative of an oral cancer, wherein if the test expression profile substantially matches a signature expression profile indicative of an oral cancer, the patient has the oral cancer.

The specification provides both working examples and sufficient descriptions of the method as recited in amended claim 1 (see, e.g., working examples on pages 69-80). Applicants believe the claim amendments have obviated the written description rejection. One of skill in the art would readily appreciate that Applicants were in possession of the claimed invention at the time this application was filed in view of the teachings of the specification.

Accordingly, Applicants respectfully request reconsideration and withdrawal of all rejections for lack of written description.

Claim Rejections under 35 U.S.C. § 112, First Paragraph

Claims 1, 5-6, and 8-11 are rejected for alleged lack of enablement. Applicants respectfully traverse this rejection to the extent it is maintained over the claims as amended.

Specifically, the Examiner asserts that "[t]he present claims do not provide any structural limitations regarding the genes utilized in the method, do not limit the type of oral disease, and do not provide any structural information regarding the expression profiles (i.e. test or signature). Accordingly, the claims encompass all known and unknown genes, all known and unknown oral diseases, and all known and unknown expression profiles." Office Action, page 10, lines 1-7.

As described above, Applicants have amended independent claim 1 to specify that the oral disease is an oral cancer and the plurality of genes are selected from Table 1. Applicants believe the claim amendments have obviated the enablement rejection. The specification amply teaches the claimed method and also provides working examples to show how to practice the claimed method. Applicants submit that the pending claims are enabled throughout their scope.

Accordingly, Applicants respectfully request that the Examiner reconsider and withdraw the enablement rejection.

Claim Rejections under 35 U.S.C. § 112, Second Paragraph

Claims 1, 5-6, and 8-11 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. Solely to expedite prosecution, Applicants have amended certain claims. Such amendments are not made in acquiescence of the rejection, and Applicants reserve the right to prosecute claims of similar or differing scope.

a. The Examiner asserts that the term "point of care" in claim 1 is indefinite. Solely for greater clarity, Applicants have amended claim 1 to remove the phrase "point of care," rendering the rejection moot.

b. The Examiner asserts that the term "signature expression profile" in claim 1 is indefinite because it is not clear whether a signature expression profile is from a patient known to have an oral disease or a normal donor and it is not clear whether the signature expression profile has 1, 2, 4, 8, 16, 32, et. genes.

Applicants respectfully disagree. Claim 1 as amended clearly specifies that the signature expression profile is indicative of an oral cancer and the plurality of genes for such signature expression profile are selected from Table 1. In addition, the specification describes that a signature expression profile is from patients known to have an oral disease. For example, the specification teaches that "Applicants have discovered a set of genes that are differentially expressed in oral cancer cells versus normal cells. Applicants have shown that the expression profile of this set of genes is indicative of oral cancer, and as such, constitutes a signature expression profile of oral cancer. Thus, measuring expression levels of these genes in a sample cell population allows for the type and tumor stage of the cells in the sample to be determined" (see, e.g., page 5, lines 5-10; and working examples). Further, the specification describes that the signature expression profile may be from either the 45 genes in Table 1 or a subset of the 45 genes in Table 1 (see, e.g., page 12, lines 5-18). In light of the teachings of the specification, the expression "signature expression profile" is not ambiguous to one of skill in the art.

c. The Examiner asserts that claim 10 is indefinite because it is unclear how assaying biological samples including bone marrow aspirates, bone marrow biopsies, lymph node aspirates, and lymph node biopsies would be useful in diagnosing oral diseases. Applicants respectfully disagree. It is known in the art that oral diseases such as oral cancer could result in gene expression changes in the whole body, including tissues other than oral tissues. One of skill in the art would recognize the metes and bounds of the claimed subject matter.

d. The Examiner asserts that claim 11 is indefinite. Applicants have cancelled claim 1 without prejudice, rendering the rejection moot.

In view of the above amendments and remarks, the Examiner is respectfully requested to reconsider and withdraw all rejections under 35 U.S.C. 112, second paragraph.

Claim Rejections under 35 U.S.C. § 102(b)

Claims 1, 5-6, and 8-11 are rejected under 35 U.S.C. § 102(b) as allegedly anticipated by Hillman et al. (U.S. Patent No. 6,121,019). Applicants respectfully traverse the rejection to the extent it is maintained over the claims as amended.

Independent claim 1 as amended relates to a method for diagnosing an oral cancer in a patient, comprising: a) obtaining a biological sample from a patient; b) determining the expression level of a plurality of genes associated with an oral cancer in the biological sample, thereby producing a test expression profile; and c) comparing the test expression profile with at least one signature expression profile of the plurality of genes selected from Table 1 indicative of an oral cancer, wherein if the test expression profile substantially matches a signature expression profile indicative of an oral cancer, the patient has the oral cancer.

The standard for anticipating a claim is clearly outlined in MPEP 2131, and this standard is further supported by the Courts. “A claim is anticipated only if each and every element as set forth in the claim is found, either expressly or inherently described, in a single prior art reference.” *Verdegaal Bros. v. Union Oil Co. of California*, 814 F.2d 628, 631 (Fed. Cir. 1978).

Applicants contend that Hillman et al. fail to satisfy the criteria for anticipating the present invention. Hillman et al. describe three human cell division regulators (HCDR1, HCDR2, and HCDR3) and use of them in preventing and treating disorders associated with cell proliferation and apoptosis. However, Hillman et al. do **not** teach or suggest at least step (c) of claim 1, for example, the signature expression profile of the plurality of genes selected from Table 1 indicative of an oral cancer. Accordingly, Hillman et al. do not teach all the elements of independent claim 1 and fail to anticipate claim 1. For the same reasons, Applicants submit that all claims depending from claim 1 are not anticipated by Hillman et al.

In view of the above amendments and arguments, Applicants respectfully request reconsideration and withdrawal of the rejection under 35 U.S.C. § 102(b).

Claim Rejections under 35 U.S.C. § 102(e)

Claims 1, 5-6, and 8-11 are rejected under 35 U.S.C. § 102(e) as allegedly anticipated by Katz et al. (U.S. Patent No. 6,797,471). Applicants respectfully traverse the rejection to the extent it is maintained over the claims as amended.

Applicants contend that Katz et al. fail to satisfy the criteria for anticipating the present invention. Katz et al. describe use of gene probes for specific regions of chromosome 3 (3p21.3) and chromosome 10 (10q22) for diagnosis and prognosis of smoking related cancers. However, Katz et al. do **not** teach or suggest at least step (c) of claim 1, for example, the signature expression profile of the plurality of genes selected from Table 1 indicative of an oral cancer. Accordingly, Katz et al. do not teach all the elements of independent claim 1 and fail to anticipate claim 1. For the same reasons, Applicants submit that all claims depending from claim 1 are not anticipated by Katz et al.

In view of the above amendments and arguments, Applicants respectfully request reconsideration and withdrawal of the rejection under 35 U.S.C. § 102(e).

#### Claim Rejections under 35 U.S.C. § 102(e)

Claims 1, 5-6, and 8-11 are rejected under 35 U.S.C. § 102(e) as allegedly anticipated by Warrington et al. (U.S. Patent No. 7,108,969). Applicants respectfully traverse the rejection to the extent it is maintained over the claims as amended.

Applicants contend that Warrington et al. fail to satisfy the criteria for anticipating the present invention. Warrington et al. describe use of gene expression profiles for diagnosis of oral cancer. However, Warrington et al. do **not** teach or suggest at least step (c) of claim 1, for example, the signature expression profile of the plurality of genes selected from Table 1 indicative of an oral cancer. Accordingly, Warrington et al. do not teach all the elements of independent claim 1 and fail to anticipate claim 1. For the same reasons, Applicants submit that all claims depending from claim 1 are not anticipated by Warrington et al.

In view of the above amendments and arguments, Applicants respectfully request reconsideration and withdrawal of the rejection under 35 U.S.C. § 102(e).

**CONCLUSION**

In view of the above remarks, Applicants believe that the pending application is in condition for allowance. A Petition for a one-month of extension of time and appropriate fees are concurrently filed herewith. If an additional fee is due, please charge our Deposit Account No. 18-1945, under Order No. **MIN-P01-042** from which the undersigned is authorized to draw.

Dated: September 17, 2007

Respectfully submitted,

By 

Z. Angela Guo, Ph.D.

Registration No.: 54,144

FISH & NEAVE IP GROUP, ROPES & GRAY  
LLP

One International Place

Boston, Massachusetts 02110

(617) 951-7000

(617) 951-7050 (Fax)

Attorneys/Agents For Applicant